Relationship of visually assessed apical rocking and septal flash to response and long-term survival following cardiac resynchronization therapy (PREDICT-CRT)

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Aims
Apical rocking (ApRock) and septal flash (SF) are often observed phenomena in asynchronously contracting ventricles. We investigated the relationship of visually assessed ApRock and SF, reverse remodelling, and long-term survival in cardiac resynchronization therapy (CRT) candidates.

Methods and results
A total of 1060 patients eligible for CRT underwent echocardiographic examinations before and 12 ± 6 months after device implantation. Three blinded physicians were asked to visually assess the presence of ApRock and SF before device implantation and also their correction by CRT 12 ± 6 months post-implantation. Patients with a left ventricular (LV) end-systolic volume decrease of ≥15% during the first year of follow-up were regarded as responders. Patients were followed for a median period of 46 months (interquartile range: 27–65 months) for the occurrence of death of any cause. If corrected by CRT, visually assessed ApRock and SF were associated with reverse remodelling with a sensitivity of 84 and 79%, specificity of 79 and 74%, and accuracy of 82 and 77%, respectively. ApRock (hazard ratio [HR] 0.40, 95% confidence interval [CI] 0.30–0.53, \( P = 0.0001 \)) and SF (HR 0.45 [CI 0.34–0.61], \( P = 0.001 \)) were independently associated with lower all-cause mortality after CRT and had an incremental value over clinical variables and QRS width for identifying CRT responders. Both the absence of ApRock/SF and unsuccessful correction of ApRock/SF despite CRT were associated with a high risk for non-response and an unfavourable long-term survival.

Conclusion
A specific LV mechanical dyssynchrony pattern, characterized by ApRock and SF, is associated with a more favourable long-term survival after CRT. Both parameters are also indicators of an effective therapy.

Keywords: Apical rocking • Septal flash • Mechanical dyssynchrony • Cardiac resynchronization therapy • Survival

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Introduction

Cardiac resynchronization therapy (CRT) has become an established treatment option for patients with left ventricular ejection fraction (LVEF) of <= 35%, QRS duration of >= 120 ms, and symptomatic heart failure resistant to optimal medical therapy, but more than a third of patients fulfilling these current guideline criteria do not benefit from this costly treatment.1 Since the principal therapeutic target of CRT is resynchronization of discoordinate ventricular contraction,2 it has been hypothesized that the assessment of mechanical dyssynchrony could improve identification of patients likely to respond to CRT, irrespective of QRS duration.4–7 Over the past decade, a plethora of methods to assess mechanical dyssynchrony has been suggested, but, so far, patient selection by mechanical measures of dyssynchrony, in both wide and narrow QRS, could not provide a sufficient added value to refine or expand guideline criteria for CRT.10,11 Most of previously suggested methods are based on the analysis of timing of longitudinal myocardial velocity peaks which may not be truly reflective of mechanical events in dyssynchronously contracting ventricles,10,12 particularly in patients with ischaemic cardiomyopathy.11 Furthermore, a prospective multicentre study raised serious doubts regarding the feasibility, reproducibility, and robustness of these parameters in a routine clinical setting.8

Visual assessment of cardiac dyssynchrony by apical rocking (ApRock) is a novel approach to assess left ventricular (LV) mechanical dyssynchrony with a potential for circumventing the limitations of previously proposed parameters.11–13 ApRock is characterized by a short septal motion of the apex due to the contraction of the septum early in systole and a subsequent long motion to the lateral side during ejection due to the late lateral contraction caused by the left bundle branch block (LBBB). The early contraction of the septum can also result in its rapid short inward motion, caused by the left bundle branch block (LBBB). The early contraction of the septum can also result in its rapid short inward motion, which has been referred to as ‘septal beaking’ or ‘septal flash’ (SF) in previous publications.14,15 Both ApRock and SF are therefore direct consequences of the mechanical dyssynchrony induced by the LBBB. Their ability to characterize mechanical dyssynchrony has already been shown in prospective observational studies demonstrating their superiority to conventional parameters.15,16 ApRock and SF can be easily visually assessed on conventional two-dimensional echocardiographic images, surpassing the need for expensive software and sophisticated myocardial velocity or strain analysis.11,13,14

We initiated a multicentre observational study (PREDICT-CRT) to investigate the relationship of a simple visual assessment of ApRock and SF and their effective correction by CRT to both response and long-term survival following CRT.

Methods

Study population

We analysed data from 1060 heart failure patients treated with CRT between March 1999 and October 2012, retrospectively collected from six European centres (detailed enrolment data are provided in Supplementary data online). Inclusion criteria were LVEF of <= 35%, QRS duration of >= 120 ms, NYHA functional class II–IV, and optimal pharmacotherapy at least 3 months before CRT. Ischaemic origin of heart failure was proved by coronary angiography or by a documented history of myocardial infarction. Patients with ischaemic cardiomyopathy had undergone revascularization procedures before they were considered for CRT implantation. Patients with ischaemic heart disease unsuitable for revascularization were also included, provided that there were no angina symptoms with optimal pharmacological therapy. The time of CRT implantation, none of the candidates required surgical or interventional revascularization for symptomatic coronary disease. Inclusion further required the availability of standard two-dimensional echocardiographic image loops from the apical and parasternal windows prior to CRT implantation and 12 ± 6 months thereafter. Data on mortality were collected from medical records, by interview with the patients’ general practitioner or relatives, and/or from national death registries. For the assessment of the association of long-term survival and ApRock/SF regardless of correction by CRT, patients were followed from the time of CRT implantation; for the assessment of survival of patients with corrected, uncorrected, and no ApRock/SF, the starting point of follow-up was the time of follow-up echocardiography.

Patients’ flow through the study is shown in Supplementary data online, Figure S1. The study was approved by the ethical committee of the University Leuven which also waived the requirement to obtain informed consents due to the retrospective and non-interventional nature of the study.

Echocardiographic data acquisition and analysis

Echocardiographic data were acquired using commercially available scanners (Vivid 5, 7, and E9, GE Vingmed Ultrasound, Horten, Norway). Digitally stored image loops were analysed off-line using EchoPac workstations. Readers had only access to the greyscale image loops and were blinded to any other patient data. Baseline and post-implant data of one patient were read separately and blinded to the results of the respective other examination, but by the same reader.

Assessment of conventional echo parameters

The analysis of conventional echo parameters comprised the LV volumes and ejection fraction, which were calculated using the modified biplane Simpson method.

Visual assessment of ApRock and SF

The presence of ApRock and SF was visually assessed pre- and 12 ± 6 months post-CRT implantation. Six readers from three of the participating centres with 3–10 years of experience in echocardiography were involved. They had been trained in ApRock and SF assessment with 10 example datasets, which were not part of the study. All readings were initially performed by two readers. A blinded third reader was asked in case of disagreement, allowing a majority decision (Figure 1 and Supplementary data online, Video S1–S3).

Assessment of myocardial scar

In the participating centres, the extent and location of myocardial scar was assessed based on MRI and scintigraphy or coronary disease was excluded by a negative coronary angiogram prior to device implantation. In combination with the assessment of ApRock and SF, readers were additionally asked to consider echocardiographic signs of scar, such as akinesia or dyskinesia in thin and hyperechogenic segments for their prediction of response. These observations were noted using a modified 18-segment model of the left ventricle (three segments per wall) and the mean of the number of scarred segments identified by two readers was used.
Cardiac resynchronization therapy

All patients received a biventricular pacemaker, in 399 (40%) with defibrillator. LV pacing leads were positioned, guided by coronary venography, preferably in lateral and posterolateral venous branches. Device settings were optimized within a week of CRT device implantation based, as deemed clinically appropriate, on surface ECG and Doppler echocardiography. Patients with an LV end-systolic volume decrease of ≥15% during follow-up were regarded as responders.

Statistical analysis

Details may be found in Supplementary data online. In short, continuous data are expressed as mean ± standard deviation and groups were compared with a two-sample t-test. In case of serious deviation from normal distribution, median and interquartile range (IQR) and a Wilcoxon rank-sum test were used. Categorical data were summarized by their observed frequencies and percentages, and compared using a Fisher’s exact test. The discriminative power of ApRock for the prediction of CRT response was analysed by the area (AUC) under the receiver operating characteristic curve and its added discriminative power was tested using c-statistics. Survival rates were estimated using the Kaplan–Meier method, and differences were tested by a log-rank test. Prediction of survival was investigated using Cox regression models. Intraobserver variability was tested in 100 randomly selected patients and interobserver variability in the whole study population using Kappa statistics. All statistical tests were two-tailed, applying a significance level of 5%. Confidence intervals (CIs) are given for 95%. We used SAS for Windows (version 9.2, SAS Institute, Cary, NC, USA) and R statistical software (version 3.02, University of Auckland, Auckland, New Zealand) for our analyses.

Results

Characteristics of the study population are summarized in Table 1 and Supplementary data online, Tables S1 and S2. Intraobserver agreement for visual assessment of ApRock and SF was 93% (κ = 0.81 [CI 0.66–0.95]) and 93% (κ = 0.80 [CI 0.66–0.95]), respectively, and interobserver agreement was 86% (κ = 0.71 [CI 0.67–0.76] for both ApRock and SF).

ApRock, SF, and response to CRT

Patients who responded to CRT (58%) were more frequently women, had more often non-ischaemic cardiomyopathy, LBBB

Table 1  Baseline clinical and echocardiographic data

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<table>
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<tbody>
<tr>
<td>Age, years (n = 1058)</td>
<td>64 ± 11</td>
</tr>
<tr>
<td>Female sex, n (%) (n = 1060)</td>
<td>255 (24)</td>
</tr>
<tr>
<td>NYHA functional class (n = 1019)</td>
<td>2.9 ± 0.5</td>
</tr>
<tr>
<td>Ischaemic aetiology, n (%) (n = 1048)</td>
<td>455 (43)</td>
</tr>
<tr>
<td>QRS width, ms (n = 974)</td>
<td>170 ± 29</td>
</tr>
<tr>
<td>LBBB, n (%) (n = 976)</td>
<td>862 (88)</td>
</tr>
<tr>
<td>Atrial fibrillation, n (%) (n = 1038)</td>
<td>261 (25)</td>
</tr>
<tr>
<td>ACEi/ARB, n (%) (n = 957)</td>
<td>920 (96)</td>
</tr>
<tr>
<td>β-blockers, n (%) (n = 965)</td>
<td>888 (92)</td>
</tr>
<tr>
<td>Aldosterone antagonists, n (%) (n = 959)</td>
<td>721 (75)</td>
</tr>
<tr>
<td>LVEF, % (n = 883)</td>
<td>27 ± 7</td>
</tr>
<tr>
<td>Left ventricular end-systolic diameter, mm (n = 918)</td>
<td>60 ± 21</td>
</tr>
<tr>
<td>Left ventricular end-diastolic diameter, mm (n = 929)</td>
<td>68 ± 10</td>
</tr>
<tr>
<td>Left ventricular end-systolic volume, mL (n = 883)</td>
<td>164 ± 71</td>
</tr>
<tr>
<td>Left ventricular end-diastolic volume, mL (n = 883)</td>
<td>223 ± 84</td>
</tr>
<tr>
<td>Scar burden, segments</td>
<td>0.78 ± 1.94</td>
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</table>

ACEi/ARB, angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker; NYHA, New York Heart Association.

Figure 1  Typical sequence of mechanical (top panels) and electrical (bottom panel) events in LBBB. An early electrical activation of the septum results in a short initial septal contraction and causes the apex to move septally while the septum moves leftward (SF, yellow arrow in the middle panel). The delayed activation of the lateral wall pulls then the apex laterally during the ejection phase while stretching the septum. This typical sequence of the septal-to-lateral apex motion is described as ‘ApRock’. The septal inward motion is described as ‘SF’.
morphology, and wider QRS complexes (see Supplementary data online, Table S3). ApRock was observed in 64% of patients (vs. 63% for SF)—among these, both ApRock and SF were observed in 83% of patients, whereas either SF or ApRock alone was seen in 8.4 and 8.6% of patients, respectively. A volumetric response rate was 77% when both ApRock and SF were present, 69% if only ApRock was seen and 56% if only SF was present.

Patients with ApRock/SF were younger, more frequently female, had more often LBBB morphology and greater QRS duration, less ischaemic disease, and less atrial fibrillation. Of note, ApRock was observed in 69% of patients with LBBB (vs. 70% for SF), and 76% of these responded to CRT (vs. 75% for SF). Only 18% of patients with LBBB were volumetric responders (83% male, 76% in sinus rhythm, 61% non-ischaemic HF, and 77% in NYHA III class) if neither ApRock nor SF was observed. In addition, ApRock was observed in 26% of patients without LBBB (vs. 20% for SF), most of whom (63% with ApRock and 62% with SF) responded to CRT.

ApRock and SF were not corrected by CRT in 9 and 8% of patients, respectively, most of whom (80 and 70%, respectively) did not respond to CRT. Patients with uncorrected ApRock had lower LVEF (26% of patients without LBBB (vs. 20% for SF), most of whom (63% for SF)—among these, both ApRock and SF were observed in 64% of patients, whereas either SF or ApRock alone was seen in 8.4 and 8.6% of patients, respectively. A volumetric response rate was 77% when both ApRock and SF were present, 69% if only ApRock was seen and 56% if only SF was present.

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ApRock corrected by CRT was highly sensitive (84%, CI 80–88%) and specific (79%, CI 73–83%) for identifying volumetric response to CRT (AUC 0.82, CI 0.79–0.85, P < 0.001). Likewise, if corrected by CRT, SF showed a good sensitivity (79%, CI 75–83%) and specificity (74%, CI 69–79%) for predicting response to CRT (AUC 0.77, CI 0.73–0.80, P < 0.001).

ApRock corrected by CRT had a significant incremental value over clinical variables (age, gender, presence of LBBB, NYHA class, ischaemic aetiology, atrial fibrillation, QRS width, baseline LVEF, and LVEDD) for the prediction of CRT response. The c-statistic index for a prediction model increased significantly by adding ApRock (0.69 vs. 0.82; change in the c-statistic 0.134, CI 0.100–0.168, P < 0.001; Figure 2 and Supplementary data online, Table S4). Similar data on SF are provided in Supplementary data online, Figure S2 and Table S5.

**ApRock and long-term survival following CRT**

During a median follow-up of 46 months (IQR 27–65), 236 (25%) of 943 patients died. Furthermore, 72 patients (6.8%) died during the first 12 months of CRT implantation. These patients had similar baseline LVEF (26 ± 6 vs. 26 ± 7, P = 0.743) and QRS width (166 ± 36 vs. 170 ± 29 ms, P = 0.397) as those who lived >12 months, but were older (mean age 67 ± 12 vs. 64 ± 11 years, P = 0.025), and more frequently had atrial fibrillation (44 vs. 24%, P = 0.001) and ischaemic origin of cardiomyopathy (58 vs. 42%, P = 0.001). This subgroup of patients also showed a lower prevalence of LBBB (72 vs. 89%, P < 0.001) and ApRock (44 vs. 65%, P = 0.002).

The vital status was available in all patients, but 118 patients (in case of ApRock) and 116 patients (in case of SF) were excluded from survival analysis due to unavailability of corresponding dyssynchrony assessment either on baseline or on follow-up visit. The baseline characteristics of these patients and the comparison with the rest of the study population are shown in Supplementary data online, Table S6. Importantly, patients excluded from survival analysis due to missing dyssynchrony assessments had survival rates similar to those included into analysis (see Supplementary data online, Figure S3). Patients with ApRock/SF before CRT implantation had a significantly more favourable overall survival than those without (log-rank P < 0.001; Figure 3A). Our data indicate further that patients with successfully corrected ApRock had a significantly more favourable overall survival than both those without ApRock and those retaining ApRock despite CRT (log-rank P < 0.001 for both; Figure 3A). Of note, there was no significant difference in long-term outcome between the latter two groups (log-rank P = 0.864).

Cox proportional hazards analysis identified ApRock, age, female sex, NYHA class, β-blocker use, and baseline LVEF as parameters independently associated with all-cause mortality (Table 2). Data on relationship of SF and long-term survival are provided in Supplementary data online, Tables S7, S8, and Figure S4A. Continuous net reclassification improvement of all-cause mortality risk for both corrected ApRock and SF is shown in Supplementary data online, Table S8.

To compare the added value of ApRock correction over LV reverse remodelling to predict the course of disease after the first follow-up visit, volumetric response to CRT was added to the multivariate model with corrected ApRock. In this test, response to CRT reached an HR of 0.533; 95% CI 0.375–0.757; P = 0.0005, without significantly affecting HR of corrected ApRock (HR 0.405; 95% CI 0.283–0.579; P < 0.0001). Similar data were obtained for SF (HR 0.465; 95% CI 0.338–0.638; P < 0.0001) and reverse remodelling (HR 0.480; 95% CI 0.342–0.675; P < 0.0001).
ApRock and SF in patients with a QRS duration of <150 ms

Separate analysis was performed to examine the potential of ApRock and SF to identify CRT responders among patients with QRS width below 150 ms ($n = 194$). The prevalence of ApRock in this subgroup of patients was 41% (vs. 37% for SF), and if corrected by CRT, it identifies volumetric responders to CRT with a sensitivity of 76% (CI 66–85%) and a specificity of 88% (CI 79–94%; AUC 0.83).
CI 0.76–0.90, \( P < 0.001 \)). Similarly, SF corrected by CRT results in a sensitivity of 69% (CI 58–79%) and a specificity of 89% (CI 80–95%; AUC 0.77, CI 0.70–0.85, \( P < 0.001 \)).

Similar to patients with QRS of \( \geq 150 \) ms, patients with QRS of \( < 150 \) ms and corrected ApRock or SF had a more favourable overall survival than both those without ApRock or SF and those retaining ApRock or SF after CRT (log-rank: for ApRock \( P = 0.0019 \) and for SF \( P = 0.0013 \); Figure 4B and Supplementary data online, Figure S4B). Also, in patients with both wide and intermediate QRS, corrected ApRock or SF was associated with lower all-cause mortality (Figure 5 and Supplementary data online, Figure S5).

### Discussion

In one of the largest series of heart failure patients undergoing echocardiographic dyssynchrony evaluation prior to CRT implantation, we investigated the association of visual assessment of ApRock and SF on routine echocardiograms and long-term survival. Our findings demonstrate that visually assessed ApRock and SF, as surrogate markers of mechanical dyssynchrony, are strongly associated with both volumetric response and favourable long-term survival after CRT. We also found that not only the presence but also the correction of ApRock and SF was the prerequisite for a lower all-cause mortality after CRT. Our data show further that the observed correction of ApRock during the first follow-up visit has a higher predictive value for further patient outcome than LV reverse remodelling. This is in agreement with earlier studies.\(^{19}\)

Although several other studies had suggested advantages in patient outcome,\(^{4,16,20–25}\) current clinical guidelines do not recommend the assessment of mechanical dyssynchrony in CRT candidates.\(^{1}\) Despite criticism regarding its methodology,\(^{26,27}\) the PROSPECT trial\(^{8}\) had caused many concerns about the accuracy and reproducibility of echocardiographic methods to detect mechanical dyssynchrony. The results of the present study strongly support the association between LV mechanical dyssynchrony and long-term outcome after CRT, and show that our visual assessment approach might surpass the limitations of dyssynchrony measurements addressed in the previous studies.

The majority of previously proposed echocardiographic parameters are derived from tissue-Doppler-based time-to-peak-

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**Table 2** Univariate and multivariate regression analyses to identify parameters associated with all-cause mortality

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Univariate HR [95% CI]</th>
<th>P-value</th>
<th>Multivariate HR [95% CI]</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ApRock (yes/no)</td>
<td>0.346 [0.272–0.441]</td>
<td>&lt; 0.0001</td>
<td>0.400 [0.304–0.526]</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Female sex</td>
<td>0.501 [0.363–0.693]</td>
<td>&lt; 0.0001</td>
<td>0.700 [0.494–0.992]</td>
<td>0.0452</td>
</tr>
<tr>
<td>LBBB</td>
<td>0.575 [0.399–0.829]</td>
<td>0.0030</td>
<td>0.690 [0.426–1.115]</td>
<td>0.1296</td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.037 [1.024–1.051]</td>
<td>&lt; 0.0001</td>
<td>1.028 [1.014–1.042]</td>
<td>0.0001</td>
</tr>
<tr>
<td>NYHA functional class</td>
<td>1.852 [1.416–2.424]</td>
<td>&lt; 0.0001</td>
<td>1.734 [1.321–2.277]</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>QRS width (ms)</td>
<td>0.998 [0.993–1.002]</td>
<td>0.3071</td>
<td>0.999 [0.994–1.004]</td>
<td>0.7967</td>
</tr>
<tr>
<td>Ischaemic aetiology</td>
<td>1.951 [1.533–2.483]</td>
<td>&lt; 0.0001</td>
<td>1.261 [0.948–1.678]</td>
<td>0.1109</td>
</tr>
<tr>
<td>Scar burden (scarred segments)</td>
<td>1.103 [1.039–1.171]</td>
<td>0.0013</td>
<td>0.991 [0.923–1.064]</td>
<td>0.7950</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1.586 [1.221–2.062]</td>
<td>0.0006</td>
<td>1.272 [0.961–1.684]</td>
<td>0.0921</td>
</tr>
<tr>
<td>( \beta )-blockers</td>
<td>0.549 [0.369–0.817]</td>
<td>0.0031</td>
<td>0.626 [0.412–0.950]</td>
<td>0.0279</td>
</tr>
<tr>
<td>ICD</td>
<td>1.093 [0.839–1.424]</td>
<td>0.5114</td>
<td>0.867 [0.643–1.169]</td>
<td>0.3490</td>
</tr>
<tr>
<td>LVEF at baseline (%)</td>
<td>0.990 [0.970–1.010]</td>
<td>0.3206</td>
<td>0.972 [0.950–0.994]</td>
<td>0.0146</td>
</tr>
<tr>
<td>LVEDD at baseline (mm)</td>
<td>0.998 [0.986–1.010]</td>
<td>0.7286</td>
<td>1.004 [0.989–1.020]</td>
<td>0.5787</td>
</tr>
</tbody>
</table>

Missing data are accounted for using multiple imputation, so all 1060 patients are included in the analysis.

CI, confidence interval; ICD, implantable cardioverter defibrillator; HR, hazard ratio; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic diameter; NYHA, New York Heart Association.

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**Figure 5** Long-term survival following CRT in patients with wide (\( \geq 150 \) ms) and intermediate (\( < 150 \) ms) QRS duration. Correction of ApRock by CRT was associated with better survival in patients with both wide and intermediate QRS duration.
velocity measurements and may also detect dyssynchrony in the presence of heterogeneous intraventricular activation sequences not treatable by CRT. In contrast to this, ApRock and SF are epi-phenomena, specific for a typical LBBB-induced contraction pattern of the LV, which may explain that their predictive value for CRT response is superior. While the concept of ApRock and SF is different from that of tissue-Doppler-derived dyssynchrony para- meters, it may be comparable with that of other, recently proposed quantitative dyssynchrony parameters reflective of LBBB-induced motion pattern, such as regional strain pattern analysis, anterosep- tal to posterior time-to-peak radial strain difference, and poten- tially also to cross-correlation analysis.

Our data imply that a trained human eye can easily detect a typical early septal movement and a septal-to-lateral apical motion pattern induced by an LBBB. Visual function assessment is not uncommon among experienced echocardiographers. It correlates well with formal methods of quantification and is in several fields (i.e. stress echocardiography), even the guideline-recommended method for decision-making. Nevertheless, clinical utility of ApRock and SF could potentially be limited by interobserver disagreement, which is most often observed in patients with borderline dyssynchrony. In such cases, a low-dose dobutamine challenge may be used to unmask or potentiate LV dyssynchrony.

The current study showed that mechanical dyssynchrony, as indi-cated by ApRock and SF, was strongly associated with a lower mor-tality after CRT, but also confirmed that reasons other than the lack of mechanical dyssynchrony might be responsible for non-response to CRT. Patients with male gender, ischaemic cardiomyopathy, and higher NYHA class were less likely to benefit from CRT. Furthermore, we observed 18% of volumetric responders among patients with LBBB and no ApRock and SF. However, the observed unfavourable response and survival of patients retaining ApRock and SF despite CRT suggest that correction of mechanical dyssynchrony is, indeed, the primary therapeutic principle behind CRT and under-lines the need for dyssynchrony assessment during CRT patient follow-up. The reasons for failures of CRT to correct ApRock were not investigated in this study and it can only be speculated that lead dysfunction, advanced heart failure, suboptimal lead place-ment, and insufficient biventricular pacing were the potential rea-sons. Nevertheless, according to our data, patients with ineffective resynchronization are at high risk for unfavourable out-come. The potential benefit of CRT optimization or reimplantation (e.g. surgical epicardial LV lead implantation) in this subset of pa-tients may be concluded from experience with individual patients, but remains to be proved.

Clinical implications

Only strong evidence from randomized trials demonstrating superi-ority of mechanical dyssynchrony over routine ECG-based criteria could change current patient selection for CRT. However, random-ized trials to clarify this point are considered unethical due to a relatively high plausibility of response in patients with a very wide QRS width (≥ 150 ms). On the other hand, the need for a bet-ter patient selection in a subgroup with an intermediate QRS dur-ation was clearly underlined by a recent meta-analysis of the five randomized CRT trials, suggesting that patients with QRS of 120–149 ms would not benefit from CRT. Our data not only demon-strated an association of ApRock/SF and better long-term survival, but also showed that ApRock and SF were able to identify respon-sers to CRT among patients with QRS duration of < 150 ms with a fair sensitivity and an excellent specificity. However, a randomized trial or retrospective analysis of previous randomized trials investigat-ing the predictive power of ApRock and SF for CRT response in this subgroup of patients is needed before the refinement of clinical practice guidelines by the assessment of mechanical dyssynchrony can be suggested. Finally, our data show that inefficient CRT is asso-ciated with worse outcome. This suggests that the assessment of mechanical dyssynchrony before and after CRT to identify and treat such patients could be of added clinical value.

Study limitations

This study was not randomized, and the relationship of ApRock and SF and, therefore, the treatment outcome in patients who did not undergo CRT remain unknown. Furthermore, although the scar burden was expectedly associated with an unfavourable outcome, our data suggest that myocardial infarct scar assessment based on echocardiography alone is suboptimal and should possibly be complemented by imaging modalities with higher accuracy for detecting scar. Using contrast-enhanced cardiac magnetic reson-ance imaging, we recently showed that myocardial scar burden is an important determinant of response to CRT. More recently, we could show that LV motion patterns are dominated by conduc-tion delays, but also modulated by infarct scar resulting in less pronounced ApRock in patients with a high scar burden. Furthermore, volumetric response to CRT among patients without ApRock/SF could be explained by other approaches for assessing cardiac dyssynchrony, including LV filling patterns, LV pre-ejection time, and interventricular mechanical dyssynchrony, which were not the part of this study.

Finally, analysis of other factors known to influence CRT re-sponse, such as discordant LV lead position and myocardial scar in the region of the LV pacing lead, was not part of this study.

Conclusions

A specific LV mechanical dyssynchrony pattern, characterized by ApRock and SF, is associated with a more favourable long-term sur-vival after CRT. Both parameters are also indicators of an effective therapy.

Supplementary data

Supplementary data are available at European Heart Journal – Cardio-vascular Imaging online.

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